

Claims

1. A method for stimulating an immune response in a subject, comprising:  
administering to a subject exposed to an antigen an effective amount for inducing a  
5 synergistic antigen specific immune response of an immunopotentiating cytokine and an  
immunostimulatory CpG oligonucleotide having a sequence including at least the following  
formula:



wherein the oligonucleotide includes at least 8 nucleotides wherein C and G are unmethylated  
10 and wherein  $X_1$  and  $X_2$  are nucleotides.

2. The method of claim 1, wherein the cytokine is selected from the group consisting  
of GM-CSF, IL-3, IL-5, IL-12, and interferon- $\gamma$ .

3. The method of claim 1, wherein the immunopotentiating cytokine is an antigen-  
cytokine fusion protein.

4. The method of claim 3, wherein the antigen-cytokine fusion protein is an antigen-  
GM-CSF fusion protein.

20 5. The method of claim 1, wherein the antigen is selected from the group consisting  
of a tumor antigen, a microbial antigen, and an allergen.

6. The method of claim 5, wherein the antigen is a tumor antigen.

25 7. The method of claim 1, wherein the antigen is administered to the subject in  
conjunction with the immunostimulatory CpG oligonucleotide and the immunopotentiating  
cytokine.

30 8. The method of claim 1, wherein the subject is passively exposed to the antigen.

9. The method of claim 1, wherein the subject has a neoplastic disorder.

10. The method of claim 1, wherein the subject has a viral infection.

11. A composition, comprising:

an effective amount for synergistically activating a dendritic cell of an

5 immunostimulatory CpG oligonucleotide having a sequence including at least the following formula:

5' X<sub>1</sub>CGX<sub>2</sub> 3'

wherein the oligonucleotide includes at least 8 nucleotides wherein C and G are unmethylated and wherein X<sub>1</sub> and X<sub>2</sub> are nucleotides, and

a cytokine selected from the group consisting of GM-CSF, IL-4, TNF $\alpha$ , Flt3 ligand, and IL-3.

*12*

11. The composition of claim 10, wherein the cytokine is GM-CSF.

*13*

12. The composition of claim 10, further comprising an antigen.

*14*

13. The composition of claim 12, wherein the antigen is selected from the group consisting of a cancer antigen, a microbial antigen, and an allergen.

*15*

14. A method for activating a dendritic cell, comprising:

20 contacting a dendritic cell exposed to an antigen with an effective amount for synergistically activating a dendritic cell of an immunopotentiating cytokine and an immunostimulatory CpG oligonucleotide having a sequence including at least the following formula:

25 5' X<sub>1</sub>CGX<sub>2</sub> 3'

wherein the oligonucleotide includes at least 8 nucleotides wherein C and G are unmethylated and wherein X<sub>1</sub> and X<sub>2</sub> are nucleotides.

*16*

15. The method of claim 14, wherein the cytokine is selected from the group consisting of GM-CSF, IL-3, IL-5, IL-12, and interferon- $\gamma$ .

*17*

16. The method of claim 14, wherein the antigen is a tumor antigen.

*110  
111  
112  
113  
114  
115  
116  
117  
118  
119  
120  
121  
122  
123  
124  
125  
126  
127  
128  
129  
130  
131  
132  
133  
134  
135  
136  
137  
138  
139  
140  
141  
142  
143  
144  
145  
146  
147  
148  
149  
150  
151  
152  
153  
154  
155  
156  
157  
158  
159  
160  
161  
162  
163  
164  
165  
166  
167  
168  
169  
170  
171  
172  
173  
174  
175  
176  
177  
178  
179  
180  
181  
182  
183  
184  
185  
186  
187  
188  
189  
190  
191  
192  
193  
194  
195  
196  
197  
198  
199  
200  
201  
202  
203  
204  
205  
206  
207  
208  
209  
210  
211  
212  
213  
214  
215  
216  
217  
218  
219  
220  
221  
222  
223  
224  
225  
226  
227  
228  
229  
230  
231  
232  
233  
234  
235  
236  
237  
238  
239  
240  
241  
242  
243  
244  
245  
246  
247  
248  
249  
250  
251  
252  
253  
254  
255  
256  
257  
258  
259  
2510  
2511  
2512  
2513  
2514  
2515  
2516  
2517  
2518  
2519  
2520  
2521  
2522  
2523  
2524  
2525  
2526  
2527  
2528  
2529  
2530  
2531  
2532  
2533  
2534  
2535  
2536  
2537  
2538  
2539  
2540  
2541  
2542  
2543  
2544  
2545  
2546  
2547  
2548  
2549  
2550  
2551  
2552  
2553  
2554  
2555  
2556  
2557  
2558  
2559  
2560  
2561  
2562  
2563  
2564  
2565  
2566  
2567  
2568  
2569  
2570  
2571  
2572  
2573  
2574  
2575  
2576  
2577  
2578  
2579  
2580  
2581  
2582  
2583  
2584  
2585  
2586  
2587  
2588  
2589  
2590  
2591  
2592  
2593  
2594  
2595  
2596  
2597  
2598  
2599  
25100  
25101  
25102  
25103  
25104  
25105  
25106  
25107  
25108  
25109  
25110  
25111  
25112  
25113  
25114  
25115  
25116  
25117  
25118  
25119  
25120  
25121  
25122  
25123  
25124  
25125  
25126  
25127  
25128  
25129  
25130  
25131  
25132  
25133  
25134  
25135  
25136  
25137  
25138  
25139  
25140  
25141  
25142  
25143  
25144  
25145  
25146  
25147  
25148  
25149  
25150  
25151  
25152  
25153  
25154  
25155  
25156  
25157  
25158  
25159  
25160  
25161  
25162  
25163  
25164  
25165  
25166  
25167  
25168  
25169  
25170  
25171  
25172  
25173  
25174  
25175  
25176  
25177  
25178  
25179  
25180  
25181  
25182  
25183  
25184  
25185  
25186  
25187  
25188  
25189  
25190  
25191  
25192  
25193  
25194  
25195  
25196  
25197  
25198  
25199  
25200  
25201  
25202  
25203  
25204  
25205  
25206  
25207  
25208  
25209  
25210  
25211  
25212  
25213  
25214  
25215  
25216  
25217  
25218  
25219  
25220  
25221  
25222  
25223  
25224  
25225  
25226  
25227  
25228  
25229  
25230  
25231  
25232  
25233  
25234  
25235  
25236  
25237  
25238  
25239  
25240  
25241  
25242  
25243  
25244  
25245  
25246  
25247  
25248  
25249  
25250  
25251  
25252  
25253  
25254  
25255  
25256  
25257  
25258  
25259  
25260  
25261  
25262  
25263  
25264  
25265  
25266  
25267  
25268  
25269  
25270  
25271  
25272  
25273  
25274  
25275  
25276  
25277  
25278  
25279  
25280  
25281  
25282  
25283  
25284  
25285  
25286  
25287  
25288  
25289  
25290  
25291  
25292  
25293  
25294  
25295  
25296  
25297  
25298  
25299  
252100  
252101  
252102  
252103  
252104  
252105  
252106  
252107  
252108  
252109  
252110  
252111  
252112  
252113  
252114  
252115  
252116  
252117  
252118  
252119  
252120  
252121  
252122  
252123  
252124  
252125  
252126  
252127  
252128  
252129  
252130  
252131  
252132  
252133  
252134  
252135  
252136  
252137  
252138  
252139  
252140  
252141  
252142  
252143  
252144  
252145  
252146  
252147  
252148  
252149  
252150  
252151  
252152  
252153  
252154  
252155  
252156  
252157  
252158  
252159  
252160  
252161  
252162  
252163  
252164  
252165  
252166  
252167  
252168  
252169  
252170  
252171  
252172  
252173  
252174  
252175  
252176  
252177  
252178  
252179  
252180  
252181  
252182  
252183  
252184  
252185  
252186  
252187  
252188  
252189  
252190  
252191  
252192  
252193  
252194  
252195  
252196  
252197  
252198  
252199  
252200  
252201  
252202  
252203  
252204  
252205  
252206  
252207  
252208  
252209  
252210  
252211  
252212  
252213  
252214  
252215  
252216  
252217  
252218  
252219  
252220  
252221  
252222  
252223  
252224  
252225  
252226  
252227  
252228  
252229  
252230  
252231  
252232  
252233  
252234  
252235  
252236  
252237  
252238  
252239  
252240  
252241  
252242  
252243  
252244  
252245  
252246  
252247  
252248  
252249  
252250  
252251  
252252  
252253  
252254  
252255  
252256  
252257  
252258  
252259  
252260  
252261  
252262  
252263  
252264  
252265  
252266  
252267  
252268  
252269  
252270  
252271  
252272  
252273  
252274  
252275  
252276  
252277  
252278  
252279  
252280  
252281  
252282  
252283  
252284  
252285  
252286  
252287  
252288  
252289  
252290  
252291  
252292  
252293  
252294  
252295  
252296  
252297  
252298  
252299  
252300  
252301  
252302  
252303  
252304  
252305  
252306  
252307  
252308  
252309  
252310  
252311  
252312  
252313  
252314  
252315  
252316  
252317  
252318  
252319  
252320  
252321  
252322  
252323  
252324  
252325  
252326  
252327  
252328  
252329  
252330  
252331  
252332  
252333  
252334  
252335  
252336  
252337  
252338  
252339  
252340  
252341  
252342  
252343  
252344  
252345  
252346  
252347  
252348  
252349  
252350  
252351  
252352  
252353  
252354  
252355  
252356  
252357  
252358  
252359  
252360  
252361  
252362  
252363  
252364  
252365  
252366  
252367  
252368  
252369  
252370  
252371  
252372  
252373  
252374  
252375  
252376  
252377  
252378  
252379  
252380  
252381  
252382  
252383  
252384  
252385  
252386  
252387  
252388  
252389  
252390  
252391  
252392  
252393  
252394  
252395  
252396  
252397  
252398  
252399  
252400  
252401  
252402  
252403  
252404  
252405  
252406  
252407  
252408  
252409  
252410  
252411  
252412  
252413  
252414  
252415  
252416  
252417  
252418  
252419  
252420  
252421  
252422  
252423  
252424  
252425  
252426  
252427  
252428  
252429  
252430  
252431  
252432  
252433  
252434  
252435  
252436  
252437  
252438  
252439  
252440  
252441  
252442  
252443  
252444  
252445  
252446  
252447  
252448  
252449  
252450  
252451  
252452  
252453  
252454  
252455  
252456  
252457  
252458  
252459  
252460  
252461  
252462  
252463  
252464  
252465  
252466  
252467  
252468  
252469  
252470  
252471  
252472  
252473  
252474  
252475  
252476  
252477  
252478  
252479  
252480  
252481  
252482  
252483  
252484  
252485  
252486  
252487  
252488  
252489  
252490  
252491  
252492  
252493  
252494  
252495  
252496  
252497  
252498  
252499  
252500  
252501  
252502  
252503  
252504  
252505  
252506  
252507  
252508  
252509  
252510  
252511  
252512  
252513  
252514  
252515  
252516  
252517  
252518  
252519  
252520  
252521  
252522  
252523  
252524  
252525  
252526  
252527  
252528  
252529  
252530  
252531  
252532  
252533  
252534  
252535  
252536  
252537  
252538  
252539  
252540  
252541  
252542  
252543  
252544  
252545  
252546  
252547  
252548  
252549  
252550  
252551  
252552  
252553  
252554  
252555  
252556  
252557  
252558  
252559  
252560  
252561  
252562  
252563  
252564  
252565  
252566  
252567  
252568  
252569  
252570  
252571  
252572  
252573  
252574  
252575  
252576  
252577  
252578  
252579  
252580  
252581  
252582  
252583  
252584  
252585  
252586  
252587  
252588  
252589  
252590  
252591  
252592  
252593  
252594  
252595  
252596  
252597  
252598  
252599  
2525100  
2525101  
2525102  
2525103  
2525104  
2525105  
2525106  
2525107  
2525108  
2525109  
2525110  
2525111  
2525112  
2525113  
2525114  
2525115  
2525116  
2525117  
2525118  
2525119  
2525120  
2525121  
2525122  
2525123  
2525124  
2525125  
2525126  
2525127  
2525128  
2525129  
2525130  
2525131  
2525132  
2525133  
2525134  
2525135  
2525136  
2525137  
2525138  
2525139  
2525140  
2525141  
2525142  
2525143  
2525144  
2525145  
2525146  
2525147  
2525148  
2525149  
2525150  
2525151  
2525152  
2525153  
2525154  
2525155  
2525156  
2525157  
2525158  
2525159  
2525160  
2525161  
2525162  
2525163  
2525164  
2525165  
2525166  
2525167  
2525168  
2525169  
2525170  
2525171  
2525172  
2525173  
2525174  
2525175  
2525176  
2525177  
2525178  
2525179  
2525180  
2525181  
2525182  
2525183  
2525184  
2525185  
2525186  
2525187  
2525188  
2525189  
2525190  
2525191  
2525192  
2525193  
2525194  
2525195  
2525196  
2525197  
2525198  
2525199  
2525200  
2525201  
2525202  
2525203  
2525204  
2525205  
2525206  
2525207  
2525208  
2525209  
2525210  
2525211  
2525212  
2525213  
2525214  
2525215  
2525216  
2525217  
2525218  
2525219  
2525220  
2525221  
2525222  
2525223  
2525224  
2525225  
2525226  
2525227  
2525228  
2525229  
2525230  
2525231  
2525232  
2525233  
2525234  
2525235  
2525236  
2525237  
2525238  
2525239  
2525240  
2525241  
2525242  
2525243  
2525244  
2525245  
2525246  
2525247  
2525248  
2525249  
2525250  
2525251  
2525252  
2525253  
2525254  
2525255  
2525256  
2525257  
2525258  
2525259  
25252510  
25252511  
25252512  
25252513  
25252514  
25252515  
25252516  
25252517  
25252518  
25252519  
25252520  
25252521  
25252522  
25252523  
25252524  
25252525  
25252526  
25252527  
25252528  
25252529  
252525210  
252525211  
252525212  
252525213  
252525214  
252525215  
252525216  
252525217  
252525218  
252525219  
252525220  
252525221  
252525222  
252525223  
252525224  
252525225  
252525226  
252525227  
252525228  
252525229  
252525230  
252525231  
252525232  
252525233  
252525234  
252525235  
252525236  
252525237  
252525238  
252525239  
252525240  
252525241  
252525242  
252525243  
252525244  
252525245  
252525246  
252525247  
252525248  
252525249  
252525250  
252525251  
252525252  
252525253  
252525254  
252525255  
252525256  
252525257  
252525258  
252525259  
252525260  
252525261  
252525262  
252525263  
252525264  
252525265  
252525266  
252525267  
252525268  
252525269  
252525270  
252525271  
252525272  
252525273  
252525274  
252525275  
252525276  
252525277  
252525278  
252525279  
252525280  
252525281  
252525282  
252525283  
252525284  
252525285  
252525286  
252525287  
252525288  
252525289  
252525290  
252525291  
252525292  
252525293  
252525294  
252525295  
252525296  
252525297  
252525298  
252525299  
2525252100  
2525252101  
2525252102  
2525252103  
2525252104  
2525252105  
2525252106  
2525252107  
2525252108  
2525252109  
2525252110  
2525252111  
2525252112  
2525252113  
2525252114  
2525252115  
2525252116  
2525252117  
2525252118  
2525252119  
2525252120  
2525252121  
2525252122  
2525252123  
2525252124  
2525252125  
2525252126  
2525252127  
2525252128  
2525252129  
2525252130  
2525252131  
2525252132  
2525252133  
2525252134  
2525252135  
2525252136  
2525252137  
2525252138  
2525252139  
2525252140  
2525252141  
2525252142  
2525252143  
2525252144  
2525252145  
2525252146  
2525252147  
2525252148  
2525252149  
2525252150  
2525252151  
2525252152  
2525252153  
2525252154  
2525252155  
2525252156  
2525252157  
2525252158  
2525252159  
2525252160  
2525252161  
2525252162  
2525252163  
2525252164  
252525216*

18  
17. A method for treating a subject having a neoplastic disorder, comprising:  
administering to the tumor of a subject having a neoplastic disorder an  
immunopotentiating cytokine and an immunostimulatory CpG oligonucleotide having a  
sequence including at least the following formula:

5 5' X<sub>1</sub>CGX<sub>2</sub> 3'

wherein the oligonucleotide includes at least 8 nucleotides wherein C and G are unmethylated  
and wherein X<sub>1</sub> and X<sub>2</sub> are nucleotides, in an amount effective for synergistically increasing  
survival time of the subject with respect to a subject administered the immunostimulatory  
CpG oligonucleotide or the immunopotentiating cytokine alone.

19  
18. The method of claim 17, wherein the tumor is selected from the group consisting  
of a tumor of the brain, lung, ovary, breast, prostate, colon, skin, and blood.

20  
19. The method of claim 17, wherein the immunostimulatory CpG oligonucleotide  
and the immunopotentiating cytokine are injected directly into the tumor.

21  
20. A contraceptive method, comprising:  
administering to a subject an antigen, an immunopotentiating cytokine and an  
immunostimulatory CpG oligonucleotide having a sequence including at least the following  
formula:

5' X<sub>1</sub>CGX<sub>2</sub> 3'

wherein the oligonucleotide includes at least 8 nucleotides wherein C and G are unmethylated  
and wherein X<sub>1</sub> and X<sub>2</sub> are nucleotides, wherein the antigen is an antigen selected from the  
group consisting of a gonadal cell antigen and an antigen from a cytokine or hormone required  
25 for the maintenance of a gonadal cell.

*Add A5*